

## MEDICATION SAFETY

# Adverse drug event trigger tool: a practical methodology for measuring medication related harm

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Adverse drug events continue to be the single most frequent source of healthcare mishaps, continually placing patients at risk of injury. This is not unexpected, given that drug treatment is the most common medical intervention and medication use is a highly complex, multidisciplinary, and largely manual process. Assessing the actual safety of drug use has been historically difficult, mainly because traditional methods such as chart audits and voluntary reporting of data have been shown to be expensive, insensitive, and largely ineffective for detecting mistakes in drug administration and drug related adverse clinical events (ADEs). Computerized methods for detecting ADEs, employing sentinel words or “triggers” in a patient’s medical record, are effective but expensive and require customized software linkage to pharmacy databases. This paper describes the use of the “trigger tool”, a relatively low cost and “low tech” modification of the automated technique. The adapted technique appears to increase the rate of ADE detection approximately 50-fold over traditional reporting methodologies.

Institute for Healthcare Improvement (IHI, a not-for-profit organization which pursues strategies for evidence based improvement in health care) and Premier (a healthcare alliance comprising 1600 hospitals across the US) have developed a modification of this technique for detecting ADEs which has been tested in 86 hospitals. This report describes the “trigger tool” in detail: its characteristics and utility, the way in which it was tested, and the results of the tests. The primary objectives were (1) to assess the feasibility of training individuals to use the trigger tool methodology efficiently, (2) to clarify the training requirements, and (3) to describe the extent and scope of the ADEs identified in different inpatient organizations.

### HISTORICAL PERSPECTIVE: CLASSEN’S METHODOLOGY

Classen’s original methodology consisted of an electronic ADE monitor using computer programs written for an integrated hospital information system.<sup>10–14</sup> In this system, specific events—including the ordering of certain drugs, orders for antidotes, certain abnormal laboratory values, and abrupt stop orders—serve as sentinels or “triggers” to initiate a more detailed concurrent chart audit. The ability to screen rapidly and comprehensively in near “real time” provides an opportunity to rectify processes that facilitate ADEs and reduce their impact on patients. While subsets of medication related harm may elude predictability, the rapid identification of these events may also reveal patterns likely to generate ADEs. Data collected can then be shared with providers of care to alter practice patterns and system design that are problematic.

In Classen’s reports other ADEs are detected from automated signals, the most common of which are high serum drug levels, leukopenia, and the use of antidiarrheal agents. Each time a trigger event is found in the pharmacy or physician order sheet of the medical record it is counted and referenced, and a daily report of the patients identified with possible ADEs is provided to a pharmacist for further in depth concurrent review. This purely electronic initial screening strategy accomplishes a rapid comprehensive review of a patient’s medical record. It is noteworthy that it does not require staff time, so it differs from conventional reviews that employ people to examine each element of the record.

In practice, the system recognizes that specific uses of a drug such as diphenhydramine recorded in a patient’s chart may have been secondary to an ADE. A more detailed chart review or audit is

Although previously published reports have suggested that many thousands of deaths per year are attributable to medical errors, the precise numbers remain unknown.<sup>1,2</sup> The appropriate challenge now is to proceed from debate about the magnitude of the problem to acceptance of the reality that processes within our current healthcare system are endangering and often harming patients. Medication errors and adverse drug events (ADEs) continue to be the single largest source of repetitive healthcare mishaps, continually placing patients at risk.<sup>3–6</sup> Efforts to detect these problems, including chart audits and voluntary administrative reporting of summary data, are expensive, insensitive, and largely ineffective.<sup>1,2,7–9</sup>

Classen developed a computerized methodology for detecting ADEs which used sentinel signals or “triggers” identified in a patient’s medical record by customized software linked to an electronic medical record that included the hospital pharmacy records.<sup>10–14</sup> Although this approach—called the “trigger tool method”—circumvents the labor intensive and largely ineffective standard chart reviews previously used to track ADEs, fiscal and technological constraints encountered in many hospitals limit its applicability. In an attempt to broaden its use, the

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**Box 1 Redesign team**

In January 1999 a group of pharmacists, physician administrators, clinicians, nurses and administrators began examination of the medication delivery system. Members represented a diverse group of experts in computerized pharmacy order entry (CPOE) systems, screening, and surveillance of medication errors. Their initial concerns were to clarify the terminology and focus of activity to reduce harm to patients. They continued to meet over the next 24 months, ultimately involving many organizations including the Mayo Health System, Bon Secor, Atlantic Health, Cleveland Clinic, and the University of Kentucky.

subsequently conducted by trained reviewers to determine the nature of the drug's use. If the drug was used in response to an ADE, that fact is documented, but if it was used for some other reason such as sedation, then no further action is needed. One can appreciate that the second phase of the process in which reviewers examine the medical record requires individuals who can discriminate between ADEs and other uses of medications in the medical record. Thus auditors or those reviewing the medical record must have a working knowledge of the medical environment. Importantly, even with these reviewers some interobserver variation inevitably occurs in the second phase of the detailed examination of the medical record. However, with training and a medical background,\* the variation among reviewers is minimal.

**THE NEED FOR EXPANDED TRIGGER METHODOLOGY**

The central goal of Classen's original effort was the development of a rapid and comprehensive methodology to screen for ADEs as they are a direct source of potential harm to patients. Furthermore, the provision of a platform for a new methodology of comprehensively screening medical records was attractive to many because it departed from traditional attempts to identify errors. The conventional method of sifting through the medical record to uncover errors was expensive and largely ineffective. The results were variable and the usefulness of the data was limited as errors and harm are different concepts, each requiring distinct corrective responses. Finally, the original work by Classen required expertise and capital in developing software to monitor pharmacy and medical activity. These investments limited the spectrum of healthcare facilities able to adopt this groundbreaking methodology. Thus, given the widespread recognition that ADEs remain the most common source of harm for patients, a growing consensus within health care sought a broader application of responsive solutions.

In response to this developing appreciation for the potential role of ADEs in patient harm, in January 2000 IHI and Premier convened a group of experts from many healthcare organizations to develop a model for a redesign of the medication system (box 1).

A key requirement was the development of a robust measurement tool to detect ADEs that was applicable throughout the healthcare system. A full appreciation of why

\*Medical background is a generic term used in this paper to underscore that nurses, laboratory, medical informatics, and pharmacy technicians, administrators and physicians were participants in learning the trigger tool technique. The distinction is to underscore the concept that individuals unfamiliar with the medical record or any aspect of medical practice are unlikely to become competent in the role of reviewing or auditing medical records with the trigger tool.

**Box 2 Categories of harm based on NCC MERP classifications of errors**

- Category E: harm that contributed to or resulted in temporary harm to the patient and required intervention.
- Category F: harm that contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization.
- Category G: harm that contributed to or resulted in permanent patient harm.
- Category H: harm that required intervention to sustain life.
- Category I: harm that contributed to or resulted in the death of a patient.

the effort focused on ADEs is noteworthy in that it underscores the divergence from traditional concepts of error as a surrogate for harm. An important component of the training to reduce variation is to define and identify ADEs accurately and reliably. The collaborative used the World Health Organization's definition for ADEs as "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or the modification of physiological function".<sup>15</sup> ADEs were then further examined by participants who attempted to classify them as mild, moderate, or severe. This was refined even further as the magnitude of harm suffered by a patient was then classified into subsets of data using the index of the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP; [www.nccmerp.org/dangerousabbr.htm](http://www.nccmerp.org/dangerousabbr.htm)). The NCC MERP classification has five categories (E–I) ranging from category E, defined as harm that contributed to or resulted in temporary harm that required intervention, to category I which is the most serious and is defined as harm that contributed to or resulted in the death of a patient (box 2).

This conceptual distinction is predicated on the more comprehensive definition of ADEs and their direct linkage to clinical outcomes compared with medication errors.<sup>16</sup> A medication error involves any mishap or mistake in the administration of a drug, including those that have no meaningful negative clinical effects. Error is thought to support the concept of preventability and is thus process focused. An ADE, as defined by the WHO (see above), is focused on harm to the patient and is outcome focused. Although the definition of medication errors therefore includes more events than ADEs, it fails to account for the unintended effects of drugs that are given appropriately but still have unintended negative outcomes. The concept of ADEs is therefore intended to include any and all results that place patients at risk or expose them to harm.

Importantly, the redesign team felt that, since the accuracy of the adapted trigger tool had not been validated and was unlikely to be reliable across institutions, it should not be used as a benchmarking tool between institutions. Moreover, the team was concerned that comparisons of ADE rates across institutions could be counterproductive as a benchmark, serving to cause unwarranted anxiety or inappropriate security. The team's efforts were therefore directed toward the creation of a measurement tool that could be easily understood and relatively simple to teach. The modified tool needed to be flexible enough to be useful across a diverse spectrum of healthcare facilities, including both community hospitals and academic medical centers. It was intended to serve as a standard for examining ADEs within an institution, and as such it required sufficient accuracy, reproducibility, and consistency to establish a baseline rate of ADEs and track them over time. More specifically, as an institution's leadership implements safety concepts resulting in cultural changes, a global measurement of ADEs can help to measure the effect of these efforts.

**Table 1** List of triggers and process identified

Trigger	Process identified
T1: Diphenhydramine	Hypersensitivity reaction or drug effect
T2: Vitamin K	Over-anticoagulation with warfarin
T3: Flumazenil	Oversedation with benzodiazepine
T4: Droperidol	Nausea/emesis related to drug use
T5: Naloxone	Oversedation with narcotic
T6: Antidiarrheals	Adverse drug event
T7: Sodium polystyrene	Hyperkalemia related to renal impairment or drug effect
T8: PTT >100 seconds	Over-anticoagulation with heparin
T9: INR >6	Over-anticoagulation with warfarin
T10: WBC <3000 × 10 <sup>6</sup> /μl	Neutropenia related to drug or disease
T11: Serum glucose <50 mg/dl	Hypoglycemia related to insulin use
T12: Rising serum creatinine	Renal insufficiency related to drug use
T13: <i>Clostridium difficile</i> positive stool	Exposure to antibiotics
T14: Digoxin level >2 ng/ml	Toxic digoxin level
T15: Lidocaine level >5 ng/ml	Toxic lidocaine level
T16: Gentamicin or tobramycin levels peak >10 μg/ml, trough >2 μg/ml	Toxic levels of antibiotics
T17: Amikacin levels peak >30 μg/ml, trough >10 μg/ml	Toxic levels of antibiotics
T18: Vancomycin level >26 μg/ml	Toxic levels of antibiotics
T19: Theophylline level >20 μg/ml	Toxic levels of drug
T20: Oversedation, lethargy, falls	Related to overuse of medication
T21: Rash	Drug related/adverse drug event
T22: Abrupt medication stop	Adverse drug event
T23: Transfer to higher level of care	Adverse event
T24: Customized to individual institution	Adverse event

PTT=prothrombin time; INR=international normalized ratio; WBC=white blood cells.

The IHI/Premier redesign team modified this original methodology by training medical staff to audit small numbers of charts efficiently and accurately without using electronic clinical databases, since such information is currently unavailable in many institutions. In a further attempt to broaden the tool's applicability, the number of triggers was expanded to 24 (T1–T23, the 24th trigger was left open to facilitate listing of a specific trigger at each organization to allow a degree of “customization”, see Appendix 1).

#### Pilot testing and refining the modified trigger tool

Teams of two reviewers from participating institutions tested the adapted trigger tool in an initial pilot program which aimed to test the feasibility of use and to assess the training needs for individuals using the trigger tool. The pilot teams consisting of two individuals were essential elements in the process as one of the central goals was to assess the ease and feasibility of training individuals in the use of the trigger tool methodology. Furthermore, because a key element in obtaining accurate data from the trigger tool review is the experience and training of the two individuals conducting the audit, these teams of two individuals were made up of experienced nurses, pharmacists, and physicians. Using a printed list of the 24 triggers (Appendix 1, table 1), each member of the team reviewed nurses' notes, physicians' orders, physicians' notes, pharmacy records, laboratory values, and vital signs in 10 charts, looking for each of the 24 triggers. For example, the chart might first be examined for the trigger “diphenhydramine”, an antihistamine which is of particular interest as it often represents the response of clinicians to an allergic or hypersensitivity reaction to a drug (an obvious ADE). But it is also sometimes used as a sedative or hypnotic agent. If absent, the next trigger was selected and the entire chart was reviewed again. If the trigger was found, the chart was then reviewed for the details of the occurrence of that specific trigger. If its use was in response to an ADE, the reviewer documented the ADE and classified its severity using the NCC MERP shown in box 2).

The pilot teams reported back to the redesign group within 6 weeks, and specific triggers were analyzed, new triggers added, and others discontinued depending on the feedback.

The entire process was then repeated several times over an 8 week cycle. The following standards for record review were developed:

- Reviews were done on closed charts (i.e. discharge summary and coding completed) with a minimum length of hospital stay of 2 days.
- Charts were chosen in a random fashion but excluded obstetrics and behavioral health because of short stays and the use of few medications.
- A goal of 20 minutes for a single chart review was set.
- A medication dose was defined as any administered drug that had a separate charge.
- Blood and blood products were not considered medications because the charges for blood products were not in the pharmacy portion of the billing data.
- The number of medication dosages administered was determined by financial data if available, or by counting the actual daily administration records.

The pilot teams showed that healthcare professionals could be quickly and competently instructed in trigger tool methodology; this process also validated the consistency and accuracy of the technique. Following the initial pilot testing, teams from all hospitals were personally introduced to the use of the trigger tool by the pilot redesign team. Members of the redesign team either travelled to healthcare systems and facilities to educate interested staff and oversee implementation of the audit process or gave instruction on the use of the tool at medication safety collaborative meetings sponsored by IHI or Premier. A trigger tool kit was developed with examples, standards, and explanations to complement the in-person instruction. The pilot teams found that medical professionals could be rapidly trained to use the trigger tool with consistently reproducible results.

#### Testing the trigger tool on a broader scale

To establish the use of the trigger tool on a broader scale, 86 hospitals in four different medication safety collaboratives were recruited over an 18 month period from June 1999. Training of new reviewers took an average of 30–60 minutes.

**Table 2** Summary data for each group participating in the program

Group	Hospitals (n)	Charts (n)	ADEs (n)	Doses (n)	% administered	ADE/1000
1	30	664	139	53256	22.4	2.61
2	9	1040	274	110562	24.2	2.47
3	23	823	222	87316	23.6	2.52
4	18	310	85	17662	29.3	4.81
Total	86	2837	720	268796	24.9	2.68

ADE=adverse drug event.

Data for number of hospitals, charts reviewed, ADEs identified, total number of doses of medications administered, percentage of ADEs of total charts (or admissions) reviewed, and number of ADEs per 1000 doses of medication administered. Individual hospital data from each group are not identified as it is emphasized that these are summary data. Within any group all reviews are aggregated.

Group 1 is composed primarily of community hospitals; group 2 is a mixture of large academic centers and community hospitals and represented the IHI redesign group hospitals; group 3 is a mixture of academic and community hospitals; group 4 is a mixture of academic and community hospitals with a high proportion of pediatric hospitals.

Trainers recommended that the first 10 charts should be reviewed using a “buddy system” to confirm competency in the use of the trigger tool. The buddy system paired an experienced auditor with a trainee, and the training was continued until the trainee was judged to be proficient. The training process emphasized the difference between a standard chart review and a trigger review, and took no longer than one hour per trainee. With a little experience, the review of 10 charts took 2–3 hours. Based on the time for training and review of charts, the redesign team was satisfied that the two person pilot teams consistently demonstrated the operational feasibility of the trigger and that training was relatively straightforward.

#### Feasibility of training and reporting of data

A total of 86 hospitals reviewed 2837 charts using the trigger tool methodology as outlined above. As previously noted, reviews were done on closed charts—that is, discharge summary and coding completed—with a minimum length of hospital stay of 2 days, so “real time” data entry with the patient still in the hospital was not accomplished. The hospitals were grouped as follows: group 1, primarily community hospitals; group 2, large academic centers and community hospitals that participated in the IHI redesign; group 3, non-participating academic and community hospitals; and group 4, academic and community hospitals with a higher proportion of pediatric hospitals than the other groups. The final grouping of the various organizations in groups 1–4 was based partly on the timing of their joining the medication safety collaborative as well as on its characteristics (academic versus community hospital system or pediatric). Thus, as groups joined the study at different times, their initial efforts began at distinct intervals which resulted in different groups being formed depending on the schedules and logistics of participation.

The four hospital groups reported ADEs per 1000 doses of medication administered, and the percentage of all reviewed charts with ADEs (table 2). There were differences in the use of the ADE data by the different hospital groups, even though all groups derived their ADE rates in a uniform and consistent manner. For example, only group 2 hospitals (1040 charts with 274 ADEs) classified the ADEs using the NCC MERP index, and two groups (groups 1 and 2; 1704 charts with 413 ADEs) tracked positive triggers that led to an ADE. The trigger review of all 2837 charts for all four groups revealed 720 ADEs out of a total of 268 796 medication doses delivered. ADEs per 1000 doses ranged from 2.47 to 4.81 across hospitals, with an average ADE rate per 1000 doses of 2.68. The consistency in the ADE rates per 1000 doses largely eliminated concerns of highly variable rates of ADEs being reported from different groups.

An important exercise was performed using a subset of participating hospitals (group 2, table 2) who collectively represented a group with significant experience in chart review to

**Table 3** Number of adverse drug events (ADEs) from hospitals in group 2 classified according to the NCC MERP definition of harm (see box 2)

Category	No of ADEs
E	219
F	34
G	3
H	13
I	5

detect ADEs. They attempted to establish concordance between the trigger methodology described in this report and more traditional methods of ADE identification such as incident reports, pharmacy interventions, and E codes. Of the 274 ADEs found in the charts of this group of hospitals, only five (1.8%) were identified by the more established or traditional reporting methodologies. These data suggest that training of large numbers of professionals to use the trigger tool is both achievable and results in consistent reliable data that are not obtainable by conventional methodology.

#### Scope and extent of ADEs

The subset of participating hospitals (table 2, group 2) reported ADEs per 1000 doses of medication which were then further categorized as previously described using the NCC MERP index. Use of this classification showed that the majority of ADEs fell into category E (table 3). Category E events are defined as those that required intervention but resulted in only temporary harm; these represented 219 out of 274 total events (79.9%). A smaller percentage involved more serious harm categories—for example, category I events, defined as those in which the ADE was judged to have contributed to the death of a patient, were found in five out of 274 events (1.8%); 13 of the 274 ADEs (4.7%) were category H events, defined as those that required intervention to sustain life, and in the remaining categories (E, F, and G) there were 256 ADEs (93.4% of the total).

A more detailed listing of the trigger tool audit summaries is shown in table 4. Data for groups 1 and 2 included 1704 charts and, using the 24 triggers shown in Appendix 1, a total of 2187 different triggers were found within the medical record; 413 represented true ADEs. The trigger that was most frequently positive was use of an antiemetic (T4) which was found 916 times, with 64 ADEs ascribed to its use (6.9% of total ADEs). The trigger with the highest percentage yield of ADEs was T22, an “abrupt medication stop”, which was found 248 times with 86 ADEs attributed to its use (35%). Table 4 provides a spectrum of trigger discovery coupled to ADEs ranging from T15 (lidocaine level >5 µg/ml) which occurred



**Table 4** Adverse drug events (ADEs) identified using the trigger tool from 1704 charts reviewed from groups 1 and 2

Trigger	No of positive triggers	No of ADEs
T1	248	38
T2	50	10
T3	13	10
T4	916	64
T5	81	19
T6	53	13
T7	35	7
T8	45	13
T9	8	4
T10	48	21
T11	9	3
T12	35	6
T13	10	4
T14	4	1
T15	0	0
T16	45	10
T17	1	0
T18	0	0
T19	2	0
T20	9	3
T21	176	53
T22	248	86
T23	71	32
T24	80	18

Individual triggers (shown in appendix 1) were used and summary data for each category are listed. The most common positive triggers identified were the use of diphenylhydramine, antiemetics, oversedation, and abrupt stoppage of medications. The most common ADEs involved anticoagulants, sedatives and pain medications, and antibiotics and insulin.

zero times to T4 (use of an antiemetic) which occurred 916 times with 64 ADEs (as noted above).

## DISCUSSION

This report describes a practical and efficient method for quantifying the occurrence of ADEs in inpatients. We have examined data in more than 2800 charts from 86 different hospitals with more than 268 000 separate medication doses using a trigger tool to uncover ADEs. Using teams of two healthcare professionals we found that the trigger tool can be efficiently and consistently applied to describe the extent and scope of the ADEs identified in different inpatient organizations. Such data supplement incident reports and pharmacy interventions as a way of defining the level of ADEs in an organization. Most importantly, the trigger enables organizations to monitor longitudinally the changes in ADE rates in response to strategies designed to improve clinical safety.

Professional staff were able to use the methodology effectively after receiving a modest amount of training. Training sessions included a single hour of detailed instruction during which each trainee examined 10 charts. Instructors were able to impart the fundamentals of the trigger tool and to test individual competency levels during a single session.

This report expands on the use of the trigger approach for identifying medication errors and ADEs reported previously by Classen.<sup>10-14</sup> His pioneering development of a methodology that moves beyond medication and drug events to additional clinical events such as hypotension or bleeding complications is significant, providing an information infrastructure for quantifying and ultimately intervening to improve clinical outcomes.<sup>12, 13</sup> Our efforts were directed towards creating a tool for investigating clinical events associated with harm that could be more widely applied than Classen's technology dependent instrument. To our knowledge, the methodology in our report has not been used previously. Our success in implementing this "low tech" and relatively low cost program in

hospitals across a range of healthcare systems markedly increases the potential generalizability of our findings.

An important step in the development of this methodology was the recognition that the reporting of harm related to medication use must not be confused with the reporting of medication errors, since most medication errors rarely result in harm to patients.<sup>1-3</sup> For example, under many definitions the failure to give a medication such as diazepam at exactly the correct time constitutes a medication error but, intuitively, we understand that giving the drug within 1 or 2 hours of the target dosing time is unlikely to expose the patient to harm. This understanding does not negate the importance of prompt administration of medications, but does underscore the fact that for many drugs the timing of administration allows for tolerance without compromising patient benefit and safety. In contrast, the concept of an ADE recognizes the importance of the adverse effects for the patient of drug administration, whether or not the drug was "correctly" administered.<sup>3-6</sup> Organizations that fail to recognize the difference between medication errors and ADEs may concentrate their efforts on systems that improve the accuracy of drug administration but that produce only marginal reductions in patient harm.

The identification of ADEs has traditionally occurred with incident reports, pharmacy interventions, or health care financing administration error codes. Classen *et al* described a trigger identifier within a computerized hospital information system that uncovered significantly more clinically relevant drug related events than traditional methods of detection.<sup>10-14</sup> Our data support the notion that traditional incident reports do not realistically quantify the true rate of ADEs as only five (1.8%) of the 274 identified using the trigger tool were filed as "incidents". This report expands the work of Classen by showing that the trigger, even without the use of electronic databases, can be widely used to detect clinical drug administration events associated with harm.<sup>10, 12</sup> The trigger tool can therefore realistically be expected to be useful in improving clinical processes.

The increased scope of the use of the trigger can be more readily appreciated if the definition of clinical harm is made broader. For example, the use of narrowly focused triggers such as the administration of flumazenil or naloxone as a screen for potential ADEs is only a limited application of the tool. These agents, used intravenously for competitive intravascular binding of narcotic/sedatives to reverse their clinical effects, are frequent "indicators" of ADEs. But the concept of the trigger can be expanded beyond medication related events directly to a wide range of adverse clinical outcomes such as hypotension and fluid overload, which can themselves serve as triggers for the detection of less than optimal care in different clinical environments. Such adverse events can be extremely difficult to uncover using traditional reporting methodology such as incident reports.

## Limitations

There are several potential limitations to the use of the trigger tool for quantifying ADEs. Firstly, universal agreement on accepted methodology for assessing the actual rate of ADEs is lacking. This absence of a "gold standard" for measuring the "true" rate of ADEs has created confusion and resulted in underreporting of ADEs. Perhaps the trigger methodology may gain acceptance as a technique to facilitate accurate measurement of ADEs. Furthermore, the lack of an accepted standardized methodology raises concern over variation among reviewers in the detection and reporting of ADEs. Our interobserver variation must also be recognized as a potential limitation of the trigger methodology, but the data presented which involved disparate healthcare organizations suggests that the actual variation is quite small. For example, of the four groups participating in the study, academic, pediatric and community hospitals had consistent rates of ADE detection (table 2). A closely

### Key messages

- Traditional efforts to detect ADEs, including chart audits and voluntary administrative reporting of summary data, have failed to improve patient safety.
- A modification of the computerized “trigger tool” developed by Classen to detect ADEs was tested in 86 hospitals.
- Use of the trigger tool requires minimal capital expense, it can be introduced rapidly with focused training sessions, and is reproducible across a broad spectrum of healthcare systems and institutions.
- The trigger tool has the potential to become standardized throughout large healthcare systems, serving as a reference to guide improvements in healthcare processes that affect patient outcomes and safety.

related concern is whether our methodology can be generalized across the spectrum of organizations or facilities delivering health care. This tool must be able to retain accuracy in the detection of ADEs in different systems of health care with reviewers of varying degrees of sophistication in the performance of chart audits.

The transition in methodology, reflecting a change in emphasis from quantifying medication error rates to measuring harm, opens important new opportunities for improvement. Thus, the versatility of the trigger tool enables a focused analysis of clinical events previously hidden from routine assessment and eliminates wasted effort directed towards quantifying errors. It also provides a mechanism for monitoring longitudinally the effect of changes to a system, and whether change has resulted in improvement. In the real world, the complexity inherent within the medical environment cannot entirely eliminate potential or actual harm. However, through use of this tool, participants in the Mayo Health System (and others) are successfully monitoring the effectiveness of initiatives to reduce clinical harm associated with anticoagulation (along with other medication use). The trigger can also efficiently help to detect potential high risk environments, allowing innovative corrective responses. Perhaps because of the ability of the trigger to identify, quantify, and longitudinally monitor ADEs, a full spectrum of programs can be initiated that will impact on their rates, similar to the efforts in anticoagulation use. It is reasonable to hope that, because of the effectiveness of the trigger, specific reductions in ADEs will ultimately translate into greater safety for our patients and reductions in serious medication errors.

## APPENDIX 1

### Adverse drug event chart review sheet

The adverse drug event chart review sheet is used by reviewers to identify various triggers (the sentinel words or signals listed below) that may appear in the medical record. Once any of the triggers is found in the medical record, the reviewer must then review the use of the trigger in the context of the care documented. A review of the record will enable the auditor to determine whether the trigger identifies a true ADE.

Look up each of the following drugs. What type of adverse drug reaction would result in the administration of that drug?—for example, protamine sulfate: patient would receive if s/he was given excess heparin.

- T1: Diphenhydramine (Benadryl)
- T2: Vitamin K (Aqua-mephyton)
- T3: Flumazenil (Romazicon)
- T4: Droperidol (Inapsine); ondanesron (Zofran); promethazine (Phenergan); hydroxyzine (Vistaril); trimethobenzamide (Tigan); prochlorperazine (Compazine); or metoclopramine (Reglan)
- T5: Naloxone (Narcan)
- T6: Diphenoxylate (Lomotil), loperamide (Imodium), kaopectate, pepto-bismol
- T7: Sodium polystyrene (Kayexalate)

Look up each of the following laboratory tests/results. What type of adverse drug reaction would result in these findings?

- T8: Prothrombin time (PTT) >100 seconds
  - T9: INR >6
  - T10: White blood cell (WBC) count <3000 × 10<sup>6</sup>/μl
  - T11: Serum glucose <50 mg/dl
  - T12: Rising serum creatinine
  - T13: *Clostridium difficile* positive stool
  - T14: Digoxin level >2 ng/ml
  - T15: Lidocaine level >5 ng/ml
  - T16: Gentamicin or tobramycin levels: peak >10 μg/ml, trough >2 μg/ml
  - T17: Amikacin levels: peak >30 μg/ml, trough >10 μg/ml
  - T18: Vancomycin level >26 μg/ml
  - T19: Theophylline level >20 μg/ml
- Why might each of the following findings indicate an adverse drug event has occurred?
- T20: Oversedation, lethargy, fall, hypotension
  - T21: Rash
  - T22: Abrupt medication stop
  - T23: Transfer to a higher level of care
  - T24: Customized to individual institution

### Adverse drug event chart review procedure

Read through the chart paying particular attention to the following sections:

- Discharge summary: may include adverse events
- Procedure notes (diagnostic, surgical): look at the narrative sections for adverse events
- Physician progress notes: may indicate changes in plan of care related to effects of medications
- Laboratory reports: looking for trigger laboratory results
- Physician orders or Medication Administration Records (MARs): looking for trigger medications
- Nursing flow sheets: looking for altered level of consciousness, skin rash
- Nursing/multidisciplinary progress notes: looking for oversedation, lethargy fall, hypotension, rash, nausea/vomiting, or other adverse events
- Obtain financial data in order to count both medications and individual dosages

If you find a trigger, check “yes” to indicate it was present in the chart. Then read through the appropriate parts of the chart to determine whether the finding was related to medication administration. Sometimes professional judgment will be required to make this determination. For example, a patient received an antiemetic an hour after a narcotic. If the patient continued to receive the narcotic without further antiemetic, the incidents are probably unrelated. If the patient continued to require antiemetics after narcotics, an ADE probably occurred. Some ADEs will result in more than one trigger. Use best judgement in determining the number of ADEs in that situation.

[Note: We are including adverse drug events that led to hospitalization or required transfer to the hospital in our review—for example, took medication, became hypotensive, fell, and was admitted to hospital. We are not including intentional drug overdoses as ADEs, nor is patient death considered “transferred to a higher level of care” in this review.]

### Process of investigation for positive trigger point

The chart review using trigger points can be very valuable in finding ADEs if the thought process used in the investigation is standardized. The following standardized process will be followed in the chart review.

#### Diphenhydramine

Diphenhydramine (Benadryl) is frequently used for allergic reactions to drugs but can also be ordered as a sleep aid, a preoperative/pre-procedure medication, or for seasonal allergies. If the drug has been administered, review the chart to determine if it was ordered for symptoms of an allergic reaction to a drug administered either during the hospitalization or before admission.

#### Vitamin K

Determine whether vitamin K was used as a response to a prolonged prothrombin time (PTT) or INR. If either laboratory value is high,

review the chart for evidence of bleeding. Look in the laboratory reports for a fall in hematocrit or for guaiac-positive stools. Check the progress notes for evidence of excessive bruising or a gastrointestinal bleed. Less likely, a hemorrhagic stroke or other internal bleeding might have occurred.

### Flumazenil (Romazicon)

This drug reverses benzodiazepine drugs. Determine why the drug was used. If hypotension or marked prolonged sedation occurred following benzodiazepine administration, an ADE has occurred.

### Antiemetics

Nausea and vomiting can be the result of drug toxicity or overdose, particularly in patients with impaired renal function. Drugs such as theophylline preparations frequently cause nausea and vomiting when levels are high. Antiemetics are also commonly administered to patients postoperatively or to those receiving chemotherapy. Professional judgement must be used in these situations to determine if an ADE has occurred.

### Naloxone (Narcan)

This is a powerful narcotic antagonist. If it has been used, overdosage of narcotics is a frequent finding. If it was used and the patient's condition did not change, doubt excessive narcotic administration.

### Antidiarrheals

Look for antibiotic-caused *Clostridium difficile* infections. If the *C difficile* was not ordered and significant diarrhea occurred in a patient receiving multiple antibiotics, it is likely that an ADE occurred.

### Glucose <50 mg/dl

Not all patients will be symptomatic. Just because serum glucose is low does not mean an ADE occurred. Look for associated use of insulin, oral hypoglycemic drugs, or evidence of symptoms and administration of glucose (orally or intravenous). In addition, look for signs or symptoms in the nursing notes about lethargy, shakiness, etc.

### *C difficile* positive stool

If a patient is on multiple antibiotics, this is a likely complication.

### PTT >100 seconds

This is a not infrequent occurrence when patients are on heparin. As with vitamin K, look for evidence of bleeding to determine if an ADE has occurred. Use professional judgement for patients with a high PTT receiving heparin during a surgical procedure.

### INR >6

A not infrequent occurrence when patients are on coumadin. Look for evidence of bleeding to determine if an ADE has occurred.

### WBC <3000 × 10<sup>6</sup>/μl

In some cases this will occur in response to drug administration. Follow the WBC counts throughout the admission and see what has happened. If leukopenia is related to drugs such as indomethacin, a fall in WBCs should be evident. Don't include patients currently receiving chemotherapy.

### Drug levels

With any drug level above normal, look for evidence of drug side effects. If any signs or symptoms have occurred, it is considered an ADE. Not all levels above normal will result in an ADE.

### Oversedation, lethargy, falls

Look in the physician progress notes, nursing or multidisciplinary notes for evidence of oversedation, lethargy, and falls. If found, look for a relationship between the event and administration of a sedative, analgesic, or muscle relaxant. Falls related to an ADE and resulting in the admission are included. Intentional overdose resulting in sedation is not included.

### Rash

There are many causes for a rash. Look for evidence that the rash is related to drug administration, including overuse of antibiotics resulting in yeast infections.

### Abrupt medication stop

In the order sets, whenever "hold" or "stop" medication orders appear, look for the reason this was done. Frequently it indicates an event of some kind.

### Transfer to a higher level of care

This includes either within the institution, to another institution from yours, or to your institution from another.

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